REMARKS

Claims 25-31 are now pending. Claims 32-40 have been added. Support is found in the original claims.

Election/Restriction

The requirement for election or restriction as set forth in the Office action mailed December 31, 2002 is traversed. The applicants acknowledge the Office's indication that such Office action states that the "requirement is not to be constructed as a requirement for election of species," but nonetheless question the Office's reference to "species" at least a dozen times in the four page Office action with respect to the present claims. For example, the Office referred to "three new species" on page 2, paragraph 2 of the Office action. In addition, the Office referred to SEQ ID NOS: 23, 25, and 27, as "Species I," "Species II," and "Species III" in paragraph 3 on page 2 of the Office action. As such, the Office required "restriction" among the three species. In response, the applicants have added nine dependent claims citing either SEQ ID NO: 23, 25, or 27 and gratefully acknowledge the Office's indication that "upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141," as indicated on the last paragraph on page 3 of the December 31, 2002 Office action.

35 U.S.C. § 101 and 35 U.S.C. § 112, First Paragraph Rejections

The applicants direct attention to the Utility Examination Guidelines, and more specifically the section entitled "Legal Analysis Supporting Utility Examination Guidelines, Section C. Therapeutic or Pharmacological Utility" (hereinafter "Guidelines"). As pointed out in previous

responses, the present claims are not directed to treating diseases as alleged on page 14, lines 4-6 and first full paragraph as well as page 18 of the Office action mailed June 14, 2004. The claims are directed to identifying compounds that are likely to be useful in treating disease conditions, however, so the Guidelines are applicable. The Guidelines clearly state that identifying a pharmacological activity of a compound, or providing an arsenal of chemicals having known pharmacological activities, is sufficient to show utility despite the early stage or lack of definitive proof of full effectiveness of such compounds. According to the Guidelines (Legal Analysis Section C):

> Courts have found repeatedly that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. As the CCPA held in Nelson v. Bowler:
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> > Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.
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> Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. Accordingly, Office personnel should not construe § 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans.

In contrast to such Guidelines, the Office repeatedly alleges that "further experimentation" is required to determine a corresponding disease state. See, for example, page 14, first paragraph, lines 7, 11, and 16 of the present action. As indicated above, such further experimentation is irrelevant to the claims.

Confusingly, and repeatedly, the Office suggests that the functions of T-type calcium channels are unknown. (See, *e.g.*, page 15, first paragraph, lines 3 and 7 of the present action.) In contrast, however, page 9 of the specification, for example, discloses conditions associated with calcium channels, namely: "epilepsy, migraine, ataxia, schizophrenia, hypertension, arrhythmia, angina, depression, small lung carcinoma, Lambert-Eaton syndrome and Parkinson's disease." As such, agonists or antagonists identified by the claimed methods may be used to treat such conditions. The Office has set forth no evidence to doubt the objective truth of such uses, and thus has not established a *prima facie* case of lack of utility. Please see the Guidelines, Legal Analysis, Section IID. Therefore, the identified compounds indeed have an identified pharmacological activity, which is sufficient for establishing utility. As the Guidelines mention, it is "faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals" having such activity. This, it is respectfully submitted, is what the present invention provides.

The Office alleges that there is no disclosure that Mg^{2+} or Ni^{2+} can treat a variety of diseases associated with ion channel activity. It is not clear how these ions relate to the claimed methods which are directed to identifying a compound in claims 25, 28, and 31, and those claims dependent thereon. Further, the Office misplaces the burden of establishing utility, as the Office has not set

forth evidence that Mg^{2+} or Ni^{2+} may not be used to treat the disclosed diseases associated with ion channel activity. Clarification is respectfully requested.

The Office alleges beginning on page 18 of the action that the asserted utilities are not substantial, specific, nor a "real world" use. The Utility Examination Guidelines, III.C.1, indicates "the initial assertion of a specific utility for the claimed invention creates a presumption of credibility." The claims, in one aspect, are directed to methods for identifying agonists or antagonists by virtue of the ability of the compound to activate the T-type calcium ion channel. The Office has not set forth anything more than its opinion to overcome this presumption of credibility. The applicants submit respectfully that such opinion is not adequate to overcome the applicants' presumption of utility.

Further, the Guidelines state that "[r]ejections under § 101 have been rarely sustained by Federal courts." In those cases where it was sustained, the applicant "failed to disclose any utility ... or asserted a utility that ... violated a scientific principle ... or was wholly inconsistent with contemporary knowledge in the art" (emphasis in original). The Office alleges on page 20, *et seq.*, that the utility of a T-type calcium channel α_1 subunit cannot be implicated solely from homology to known ion channels or their protein domains because a sequence's function may be erroneous based on homology. It is not clear how this discussion relates to a method to identify an agonist or antagonist using a cell which expresses an α_1 subunit of a heterologous T-type calcium channel. The α_1 subunit is defined in the claims as functioning as a T-type calcium ion channel, so there is no doubt as to the function of the α_1 subunit. Even if this allegation were relevant to the claims, the claimed function of the α_1 subunit would not be wholly inconsistent with contemporary knowledge. The applicants' asserted utility does not violate a scientific principle. Agonists or antagonists

identified by the methods of the invention are useful as having an effect on the activity of calcium ion channels. In turn, such agonists and antagonists are useful in treating conditions identified in the specification.

Finally, respectfully, the Office appears to have ignored the precedent that at least two patents have issued directed to nucleotide sequences encoding T-type channels: U.S. 6,358,706 and U.S. 6,309, 858. Obviously the art itself understands that T-type channels are useful; as claimed presently, they are useful for identifying agonists and antagonists of their activity which are in turn useful in treating a large number of conditions. This is exactly the same thing that is stated by the patentees in these issued patents. See, for example, column 6, lines 33-50, in the '706 patent and column 19, lines 53-57, of the '858 patent.

Thus, each of the presently pending claims in this application has specific, substantial and "real world" utility and is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 381092000720. However, the Commissioner is not authorized to charge the cost of the issue fee

to the Deposit Account.

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Respectfully submitted,

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